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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/241,347 02/02/99 BUJARD

H BBI-009C4CN

EXAMINER

000959
LAHIVE & COCKFIELD
28 STATE STREET
BOSTON MA 02109

HM22/0913

ART UNIT	PAPER NUMBER
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1632
DATE MAILED:

09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/241,347

Applicant(s)

BUJARD ET AL.

Examiner

Ram Shukla

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 December 1999.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4,5,7-11,13-16,18,19 and 21-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,5,7-11,13-16,18,19 and 21-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Art Unit: 1632

DETAILED ACTION

1. Amendment and response filed 12-13-99 is acknowledged.
2. Claims 3,6,17, and 20 have been cancelled.
3. Regarding, amendment to claims it is noted that the amended claims have a broader scope than the originally presented claims.
4. Amended claims 1, 2, 4, 5, 7-11,13-16, 18, 19, and 21-26 and Newly submitted claim 27-28 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 1, 2, 4, 5, 7-11,13-16, 18, 19, and 21-26 have been amended to recite a transgenic organism which encompasses any and all organisms, such as animals and plants. In fact, claim 12 has been amended to recite a transgenic plant, which are patentably distinct from the originally claimed invention of transgenic non-human animal. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Therefore, claims 1, 2, 4, 5, 7-11,13-16, 18, 19, and 21-28 encompass non-elected invention. Accordingly, claims 1, 2, 4, 5, 7-11,13-16, 18, 19, and 21-28, would be examined for a transgenic animal, the originally presented invention. Additionally, claim 12 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.
5. This application contains claim 12 drawn to a nonelected invention in view of the amendment filed 12-13-00. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Information Disclosure Statement

6. The information disclosure statement filed 12-13-99 fails to comply with 37 CFR 1.97(c) because it lacks a statement as specified in 37 CFR 1.97(e). It has

Art Unit: 1632

been placed in the application file, but the information referred to therein has not been considered.

7. The information disclosure statement filed 12-13-99 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

8. Claims 1, 2, 4, 5, 7-11, 13-16, 18, 19, and 21-28 are objected to because of the following informalities: It is noted that these claims encompass non-elected invention, i.e. transgenic organisms. Applicants are required to modify the claim language to reflect the elected invention.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-11 and 13-26 and new claims 27-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse, whose genome comprises: a first transgene comprising a transcriptional regulatory element functional in cells of the mouse operatively linked to a polynucleotide sequence encoding a fusion protein that inhibits transcription in eukaryotic cells wherein the fusion protein comprises a tet repressor or mutated tet repressor that binds to a tet operator in the absence or presence of tetracycline or tetracycline analog and that is operatively linked to a heterologous polypeptide which inhibits transcription in eukaryotic cells and a second transgene comprising a

gene of interest operatively linked to at least one tet operator sequence, wherein said gene of interest confers a detectable and functional phenotype on the mouse when expressed in cells of the mouse, wherein the level of expression of the tet-operator linked gene of interest can be upregulated by administering tetracycline or tetracycline analogue to the mouse and a method for modulating transcription of the second transgene in the transgenic animal by administering tetracycline or tetracycline analog to the animal, does not reasonably provide enablement for any other embodiment, for reasons of record set forth in the previous office action of 7-8-99. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 12-13-99 have been fully considered but they are not persuasive. With regard to "a Tet repressor or mutated Tet repressor", it is noted that applicants' arguments are moot in view of the inclusion of "a Tet repressor or mutated Tet repressor" in the enabled scope of the claimed invention. With regard to "a any and all transcriptional silencer domains", applicants' arguments are persuasive and the rejection is withdrawn.

With regard to making of any and all transgenic non-human animals, applicants' arguments are not persuasive for reasons of record set forth in the previous office action of 7-8-99. It is noted that applicants point to lines 29-31 on page 13, for support for design of expression vectors, however indicated section of the specification is just a statement and does not provide any guidance as to how to make a vector that could be used for producing transgenic cow, sheep, goat or pig. Next applicants have argued that the arts of Mullins, Hammer et al, and Seidel, in place of supporting unpredictability, rather support that different species of transgenic animals can be produced. For example, applicants argue that Hammer et al teaches successful expression of a transgene in two different species. However, applicants ignore the point that rat and mice did not show same

Art Unit: 1632

phenotype using the same transgene and this is the unpredictability issue that same transgene does not produce same phenotype in two different species. Applicants have not addressed this issue. Additionally, it is emphasized that the issue is not whether one has produced transgenic non-human animals of different species, rather the issue is: following the directions of the specification and the prior art, could an artisan have been able to produce instantly claimed transgenic non-human animals that expressed claimed transgene and produced the same phenotype or what phenotype in the animals and the the answer is: due to the unpredictability of the steps and factors of making a transgenic non-human animal, such as, gestation time, litter size, number of fertilized eggs required for micro injection, low efficiency of gene integration, method of introduction of transgenes, construction of a suitable vector, variation in expression levels, between different cell lines and species, host genetic background, the site of chromosomal insertion and absence of specific transcription factors a, an artisan would have had to carry out extensive experimentation to make the claimed transgenic non-human animals and such experimentation would have been undue. It is noted that the applicants have not addressed as to how an artisan of skill would have addressed these art recognized problems of producing a transgenic non-human animal that express a certain transgene, rather, applicants have cited articles (Hammer et al, Pursel et al, Rexroad et al, and Ebert et al) which report production of transgenic rabbits, pigs, sheep or goats. It is noted that none of these articles teach as to how an artisan of skill would have addressed the issues raised in the office action.

Applicants arguments regarding the efficacy of the tetracycline controlled gene expressing in different eukaryotic cells is persuasive.

In summary, applicants arguments are not sufficient to address all the enablement issues raised in the previous office action and therefore, the scope of the enablement rejection is maintained as discussed above.

Art Unit: 1632

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.3218 may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-11 and 13-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 5, 866,755 (2-2-1999), for reasons of record set forth in the previous office action of 7-8-99.

Response to Arguments

Applicant's arguments filed 12-13-99 have been fully considered but they are not persuasive. In response to applicants arguments, it is noted that there are two grounds for the obvious type double patenting rejection, to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. While the applicants have argued that the term of the instant application if issued would expire in June 2013, before the expiry of the patent 5,866,755, applicants have not discussed the second ground for the rejection - to prevent possible harassment by multiple assignees. Accordingly, the rejection is maintained and a terminal disclaimer in compliance with 37 CFR 1.3218 would be required to overcome the double patenting ground. See 37 CFR 1.130(b).

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c) and a copy of all the pending/under consideration claims. For instructions, Applicants are referred to <http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm>.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Kay Pinkney whose telephone number is (703) 305-3553.

Ram R. Shukla, Ph.D.


DAVE T. NGUYEN
PRIMARY EXAMINER